AWARD NUMBER: W81XWH-16-1-0302

Proposal #: PR150678

TITLE: Exploiting Inhibitory Siglecs to Combat Food Allergies

PRINCIPAL INVESTIGATOR: Michael Kulis, Ph.D.
CONTRACTING ORGANIZATION: University of North Carolina at Chapel Hill

PARTNERING INVESTIGATOR: James C. Paulson, Ph.D.

REPORT DATES: OCTOBER 2020

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	**2. REPORT TYPE**	**3. DATES COVERED**
October 2020	Annual	September 30, 2019 - September 29, 2020

4. TITLE AND SUBTITLE

Exploiting Inhibitory Siglecs to Combat Food Allergies

5a. CONTRACT NUMBER
W81XWH-16-1-0302

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

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8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES
Drs. Kulis and Paulson are partnering PIs on this award. Dr. Matthew Macauley, previous Partnering PI, has moved to the University of Alberta (Edmonton, Alberta) and continues to participate under a sub-contract from TSRI.

14. ABSTRACT
During the fourth year of this award, we have continued to generate important data related to targeting of CD22 on B cells and CD33 on mast cells to abrogate food allergies. Unfortunately, the COVID-19 pandemic shut down our labs in March 2020 for several months, causing some delays in our work. With that said, we have still produced new data and are now back in the labs on a regular basis to carry out additional experiments. For the CD22 project, we have now developed a humanized mouse model using NSG mice lacking mouse B and T cells, transfused with human PBMCs. These mice make human IgG against peanut allergens upon exposure to peanut and in pilot experiments, we were successful in stopping this IgG production by use of Ah1 STALs. We have also prepared mouse CD22L Ah1, Ah2, Ah3, and Ah6 for use in our conferred memory model to block IgE production to all major allergens. In terms of targeting CD33 in this past year, we have developed a novel approach by conjugating human CD33L directly to anti-human IgE, without the use of liposomes for scaffolding. This molecule is effective in inducing tolerance in humanized mice. Overall, our results move us closer to translating our STALs platform into human studies by focusing now on the use of humanized mouse models and human CD22 and CD33 ligands in our systems. Finally, we have applied for an Expansion Award for this project.

15. SUBJECT TERMS
Food allergy; peanut allergy; Siglec; IgE; Ara h 2; CD22; CD33; mast cell; basophil

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			USAMRMC
Unclassified	Unclassified	Unclassified	Unclassified	15	**19b. TELEPHONE NUMBER** *(include area code)*

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1. INTRODUCTION:

In this pre-clinical, translational project, we will utilize mouse models, human B cells, and human mast cells and basophils to assess the ability of Siglec-engaging Tolerance-inducing Antigenic Liposomes (STALs) to induce immunological tolerance to peanut allergens. STALs are bioengineered nanoparticles that co-display a selected antigen and high affinity Siglec ligand. STALs targeting the Siglec CD22 on B cells induce antigen-specific B cell tolerance through deletion of the B cells recognizing the antigen. Applying this approach to animals with an existing peanut allergy will allow us to deplete memory B cells responsible for producing IgE, and establish a novel therapeutic strategy for food allergies. STALs targeting the human Siglec CD33 will be used to desensitize mast cells. This approach will be investigated as a therapeutic strategy for preventing acute allergic reactions, allowing for tolerizing doses of antigen to be delivered safely. By exploiting the inhibitory functions of CD22 on B cells, and CD33 on mast cells and basophils, our primary objectives are (1) to develop a novel prophylactic and therapeutic approach for peanut allergy and (2) to develop a targeted approach to prevent mast cell and basophil degranulation to peanut allergens.

2. KEYWORDS:

Food allergy; Peanut allergy; Siglec; CD22; CD33; STAL; nanoparticle; Ara h 2; mast cell; basophil; B cell

3. ACCOMPLISHMENTS:

- **What were the major goals of the project?**

Specific Aim 1: **Establish the therapeutic potential of Ara h 2 STALs targeting CD22 to abrogate peanut allergies.**

- ***Major Task 1***: Determine optimal conditions to induce B cell tolerance to Ara h 2 and whole peanut extract in a prophylactic mouse model.
  Target date: Months 1-12; *percentage of completion*: **100%**
- ***Major Task 2***: Use Ara h 2 STALs to induce tolerance by deletion of memory B cells
  Target date: Months 10-30; *percentage of completion*: **90%**
- ***Major Task 3***: Determine translatability of STALs to human CD22 and human B cells
  Target date: Months 5-24; *percentage of completion*: **75%**

Specific Aim 2: **Demonstrate the applicability of Ara h 2 STALs targeting CD33 to prevent mast cell- and basophil-mediated allergic responses to peanut allergen.**

- ***Major Task 1***: Determine inhibitory effects and longevity or inhibition using LAD-2 mast cells
  Target date: Months 1-7; *percentage of completion*: **100%**
- ***Major Task 2***: Determine inhibitory effects and longevity of inhibition using Human Basophils
  Target date: Months 7-18; *percentage of completion*: **75%**
- ***Major Task 3***: Determine preventive effects of STALs targeting CD33 on mast cells in vivo in allergic mice
  Target date: Months 6-30; *percentage of completion*: **90%**
- ***Major Task 4***: Determine therapeutic utility of STALs targeting CD33 and CD22 simultaneously in allergic mice
  Target date: Months 18-36; *percentage of completion*: **50**%

- **What was accomplished under these goals?**

This report is for a Partnering PI project with James C. Paulson at The Scripps Research Institute (TSRI) as Partnering Investigator and Michael Kulis at the University of North Carolina (UNC) as Principal Investigator. Dr. Matthew Macauley was originally Partnering PI at TSRI and moved to the University of Alberta (UofA), where he continues in the project under a subcontract from TSRI. In this current project period, the work was conducted in the laboratories at UNC, TSRI, and UofA and accomplishments listed below we have noted which institution/investigator was involved in the experiments.

Specific Aim 1: **Establish the therapeutic potential of Ara h 2 STALs targeting CD22 to abrogate peanut allergies.**

***Major Task 1*:** Determine optimal conditions to induce B cell tolerance to Ara h 2 and whole peanut extract in a prophylactic mouse model.

Previously, we reported that prophylactic tolerization of BALB/c mice to Ara h 2 (Ah2) using a CD22-targeted approach results in complete tolerance of mice following sensitization with peanut extract followed by a challenge with soluble Ah2 (Orgel et al., JACI, 2017). In that manuscript, we also described that Ah2 STALs-treated mice were also significantly protected from a challenge with peanut extract, however, this protection was not complete. This lack of complete protection was potentially due to minor responses from the other peanut allergens, such as Ah1, Ah3, and Ah6. Accordingly, the most robust form of tolerance to peanuts would need to consider for these other allergens.

Ah1, 2, 3, and 6 STALs have been prepared, and tested in our mouse models. Ah1 and Ah2 work well, however, we are still optimizing Ah3 and Ah6 conditions. So far, there is an effect, but it is not as complete as with Ah1 and Ah2. Experiments are ongoing with these STALs in both BALB/c mice (Dr. Kulis at UNC) and in B57BL/6 mice (Dr. Macauley at UofA). The goal is to use multiple allergen STALs to completely protect mice from the whole peanut extract challenges. Additionally, we will use the B cell tetramers developed in collaboration with Justin Taylor (Fred Hutchinson Cancer Center) to track the depletion of Ah1, 2, 3, and 6 B cells in mice following STALs treatment. The tetramers have been optimized previously as discussed in last year's progress report.

***Major Task 2*:** Use Ara h 2 STALs to induce tolerance by deletion of memory B cells

During the previous reporting periods, we demonstrated the ability to suppress memory B cell responses to Ah2 in an adoptive transfer model. We are now testing the ability of Ah1, 2, 3, and 6 in combination to tolerize mice to whole peanut extract. These experiments were interrupted by the COVID-19 pandemic that shutdown our lab for several months starting in March 2020, so the experiments had to be re-started. They are ongoing now with plenty of STALs prepared and mice in-hand in our mouse facility.

***Major Task 3*:** Determine translatability of STALs to human CD22 and human B cells

Previously, we reported the development of a new human CD22 (hCD22) transgenic mouse (Bednar et al, J Immunol, 2017). We then used these mice to determine if tolerance induction of peanut allergens through hCD22 is equally as robust as through mCD22 (mCD22). We had success with Ah1 and Ah3 STALs using hCD22L, as discussed in last year's progress report. This year, we moved into a humanized mouse model system at UNC to determine the effects of STALs directly on human B cells. We used NSG mice, lacking mouse B and T cells, and repopulated the immune system using human PBMCs from peanut allergic donors. Then, using Ah1 STALs with the *human* CD22 ligand, we found a significant reduction in peanut-specific IgG responses following boost injections with peanut allergens (**Fig. 1**). We have ongoing experiments using this humanized B cell model to reproduce the Ah1 hCD22L STALs, but also expanding that to Ah2, Ah3, and Ah6 allergens. These STALs have already been prepared and we are moving along quickly with generating these data. If everything goes according to plan, we will use this human B cell data, along with our previous conferred memory B cell data on mouse B cells to write a manuscript targeting a high-impact journal. We feel that this translational approach to depleting mouse and

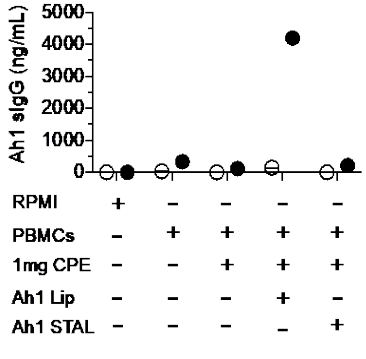

Figure 1. Ah1 STALs prevent memory recall responses from human B cells in humanized NSG mice. Open circles are pre- and closed circles are post-Ah1 boost for recall responses.

human peanut-specific B cells will be a major advancement in the field of food allergy.

Specific Aim 2: Demonstrate the applicability of Ara h 2 STALs targeting CD33 to prevent mast cell- and basophil-mediated allergic responses to peanut allergen.

Major Task 1*: *Determine inhibitory effects and longevity or inhibition using LAD-2 mast cells.

Significant Results and Achievements: This task was completed in the first year of the project as reported in the previous progress reports.

Major Task 2: Determine inhibitory effects and longevity of inhibition using Human Basophils

In the previous reporting period, we made significant advances in applying the CD33 STALs platform to human basophil assays. Dr. Macauley provided PEGylated lipid to Ah2 and shipped this to Dr. Paulson. Dr. Paulson's team then coupled the Ah2 and human CD33 ligand to liposomes, thus generating the Ah2 CD33 STALs. These data are shown below, along with descriptions of the findings. We are still pursuing this line of research and plan to publish within the next 12 months. The limitation here is getting enough blood donors to come in to generate another 5-10 data points. As with other parts of the project, this was delayed with COVID-19 and scheduling clinical appointments during Spring/Summer of 2020. However, the UNC Food Allergy Clinic is open again and we should have donors coming in soon. STALs with the hCD33L are prepared and ready for use.

Dr. Kulis tested the Ah2 CD33 STALs in two types of assays from four different peanut allergic patients. The first assay was a straight-forward test of applying either Ah2-liposomes (Ah2-LP) or Ah2 CD33 STALs (Ah2-CD33L) to whole blood from humans with peanut allergy. Basophil activation was then assessed by staining the blood for markers to identify basophils (CD123 and CD203c) and looking at CD63 as a marker of degranulation. As shown in **Figure 2**, Ah2-LP led to significantly more degranulation of basophils (%CD63+) than the Ah2-CD33L. We tested 1 µg/mL and 0.1 µg/mL doses and found similar trends for both doses. These data indicate that co-displaying CD33 ligand with Ah2 drastically decreases the amount of basophil degranulation. This finding is encouraging for further translational development of CD33 STALs in the treatment of food allergy.

The second assay was designed to test whether pre-incubation with Ah2-CD33L STALs could prevent further responses to Ah2 stimulation. We first added either PBS as a sham control, or Ah2-CD33L to whole blood from peanut allergic donors for 1 hour, then stimulated with Ara h 2 in the form of Ah2-LP. The data demonstrates that Ah2-CD33L pre-treatment dramatically reduces further degranulation in response to Ah2 (**Figure 3**). We plan to repeat this assay using several more peanut allergic donors.

We anticipate reproducing these findings and then writing a manuscript on this data in the next reporting period.

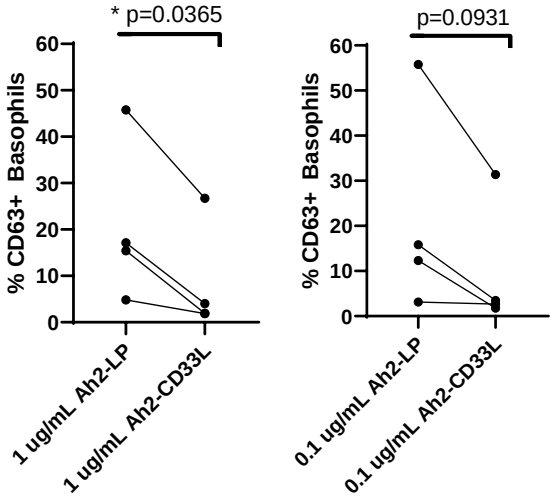

Figure 2. Whole blood basophil activation testing performed with Ah2-LP versus Ah2-CD33L. Data is shown from four individuals with peanut allergy. Ah2-CD33L has significantly lower ability to activate human basophils than Ah2-LP, indicating that CD33 ligand can suppress basophil responses.

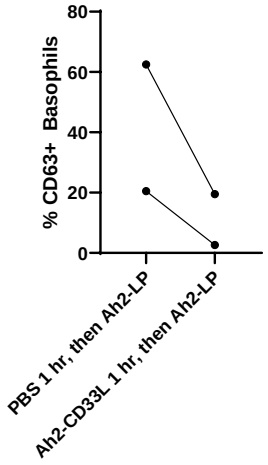

Figure 3. Whole blood human basophil activation testing with pre-treatment of Ah2-CD33L. The data indicate that pre-treatment of human basophils with Ah2-CD33L can suppress subsequent stimulation with Ah2.

Major Task 3: Determine preventive effects of STALs targeting CD33 on mast cells in vivo in allergic mice.

Significant Results and Achievements: Last year we presented major progress in demonstrating desensitization of mast cells using STALs co-presenting both CD33 ligand (CD33L) and TNP in transgenic mice expressing hCD33 on mast cells. This work is now published (Duan et al (2019) J. Clinical Invest. 129, 1387).

We have subsequently been working towards demonstrating the utility of STALs in actively sensitized mice using human CD33L on humanized mast cells in mice. Additionally, we have created a new reagent by coupling human CD33L to anti-human IgE using a linker (**Figure 4A and 4B**). This reagent binds human IgE as demonstrated by ELISA (**Figure 4C**). We compared the native anti-IgE clone HB121 (ATCC) with the linker modified (N3) and CD33L modified (CD33L) conjugates for their ability to introduce anaphylaxis in NSG-SGM3-CD34+ stem cell humanized mice sensitized 24 hours earlier with human IgE. As shown in **Fig. 5A**, native anti-IgE and N3-anti-IgE produced robust anaphylaxis, while the mice treated with the CD33L-anti-IgE were protected from anaphylaxis. In a separate experiment, mice treated with either buffer (PBS) or CD33L modified anti-IgE showed no anaphylaxis (**Fig 5B**), but when challenged 5 hours later with native anti-IgE, the PBS treated mice did not survive, while the CD33L-anti-IgE treated mice were protected, indicating that the initial treatment desensitized them to the challenge (**Fig. 5C**). In future experiments we will adjust the amount of anti-IgE in the challenge to reduce the severity of anaphylaxis and risk of animal death in the control experiments.

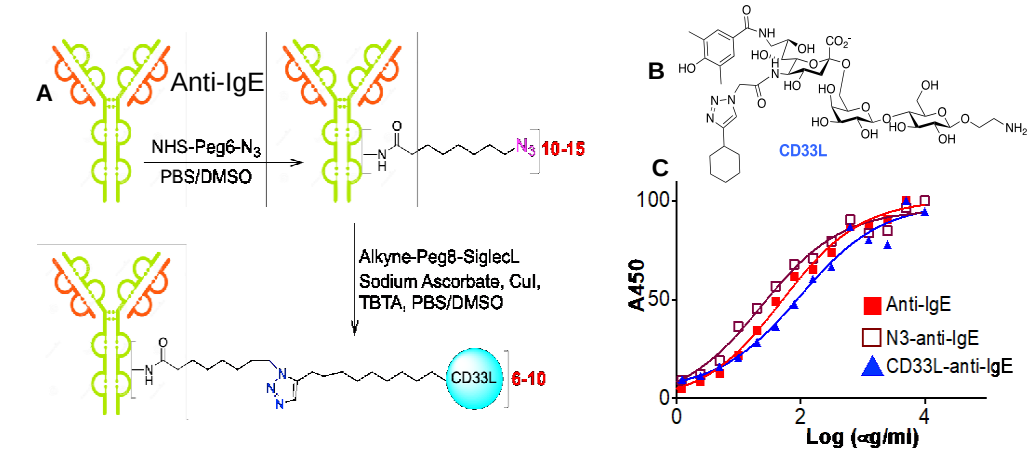

Figure 4. Conjugation of CD33 ligand to human anti-IgE. A) Linkers are chemically conjugated to lysine side chains on anti-IgE (N3-anti-IgE) and then coupled to alkyne modified CD33L (CD33L-anti-IgE). B) Structure of CD33L. C) ELISA analysis of anti-IgE binding to IgE coated on the plate.

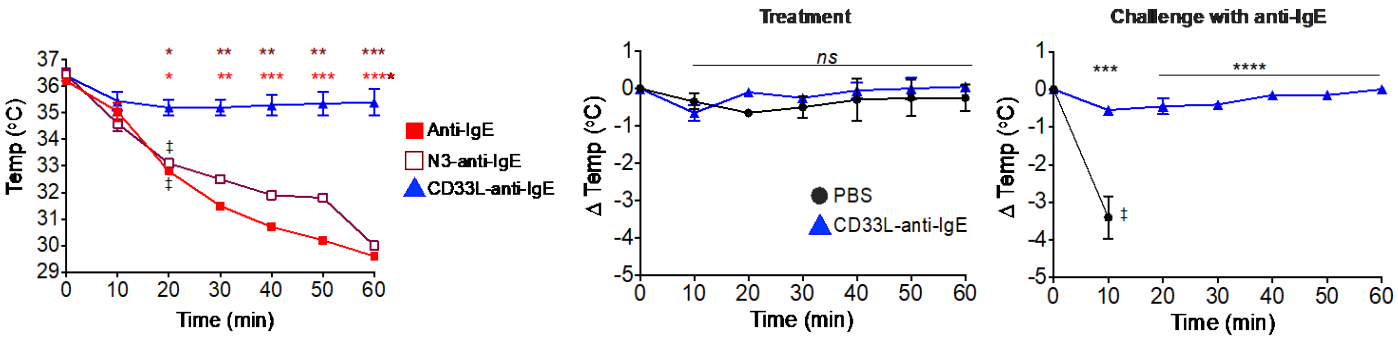

Figure 5. Anti-IgE-CD33L desensitizes NSG-SGM3-CD34+ humanized mice to anti-IgE mediated systemic anaphylaxis. Mice were sensitized with anti-OVA human IgE i.v 24 hours before testig. A) Sensitized mice (N=3) were injected with 5 µg anti IgE ± modification with linker (N3-anti-IgE) or linker and CD33L (CD33L-anti-IgE). B) Sensitized mice were treated with PBS or 5 µg CD33L-anti-IgE (left) and 5 hours later were challenged with 5 µg anti-IgE. Results in (A) were analyzed by Two-way ANOVA followed by Tukey's test (*P<0.05, **P<0.01, ***P<0.001 ****P<0.0001); Results in (B) were analyzed by Two-way ANOVA followed by Sidak's multiple test (***P=0.0002 and ****P<0.0001), ‡ indicates mice found dead.

Major Task 4: Determine therapeutic utility of STALs targeting CD33 and CD22 simultaneously in allergic mice .

Significant Results and Achievements: This Task requires sensitized mice that undergo IgE mediated anaphylaxis. We are also constrained to the C57Bl/6 strain since hCD33 is on a C57Bl/6 background. We are still working towards a robust protocol for sensitizing mice to allergen that will produce IgE mediated anaphylaxis. This is absolutely required since it is needed to show that the CD22 STALs will prevent increased production of the IgE, and that the CD33 will prevent anaphylaxis resulting from the exposure to allergens.

- **What opportunities for training and professional development has the project provided?**

  At UNC: During this reporting period, Lakeya Hardy, a graduate student in Dr. Kulis' lab, has been funded through a Graduate Diversity Enrichment Program (GDEP) fellowship sponsored by the Burroughs Wellcome Fund. The title of her project sponsored under the award is: Using STALs to exploit CD22 on peanut-specific memory B cells to induce tolerance. She is expected to publish her work on CD22 STALs in 2021 and then write her thesis and defend sometime in 2021.

  As in previous reporting periods, this work has also contributed to the development of other trainees in Dr. Kulis' group. A postdoctoral researcher (Johanna Smeekens) and two graduate students (Lakeya Hardy and Jada Suber) have been involved with the projects at UNC. Dr. Kulis is responsible for mentoring the three trainees and meets with them individually on a weekly basis to go over experimental progress. This project has allowed for training in various experimental techniques, including mouse procedures, working with

human B cells, ELISA, and flow cytometry. Additionally, all three trainees have attended two major conferences, the Gordon Research Conference on Food Allergies (January 2018) and the American Academy of Allergy, Asthma, and Immunology (March 2018), presenting their research. Other career development gained by this project have included opportunities to network with investigators at TSRI and UofA and opportunities to discuss their findings at departmental seminars at UNC.

At TSRI: An Individual Development Plan (IDPs) was updated for Shiteng Duan (Grad Student) to continue monitoring the training and progress in developing his scientific career. He received one-on-one guidance from Dr. Paulson (Mentor) on a daily basis and presented several times at regular lab meetings. He also presented his work in the form of posters/oral presentations at local and international meetings/symposiums. In May 2019 Shiteng graduated with his PhD at Scripps Research, and in August 2019 he accepted a position at the Genomics Institute of the Novartis Research Foundation in San Diego, CA.

At UofA (sub-contract to TSRI): Dr. Macauley met on a daily basis with post-doctoral fellow Gour Daskan and graduate student Kelli McCord and has provided hands on training on working with allergens, formulating liposomes, and immunizing mice. All members of our team actively participate in groups meetings and attend local GlycoNet meetings. The postdoctoral and graduate students' offices at UofA facilities many courses to assist in writing in communicating, and all trainees in the Macauley lab are encouraged to take advantage of these resources.

How were the results disseminated to communities of interest?

Scientific meetings/conference/symposia and publications (see below).

- **What do you plan to do during the next reporting period to accomplish the goals?**

At UNC

For Aim 1, Major Task 1: We will continue testing Ah1, 2, 3, and 6 in a prophylactic model using BALB/cJ mice. We will quantify allergen-specific IgE and IgG1 and will assess anaphylaxis during challenges with whole peanut extract. The STALs will be prepared by Dr. Macauley's group at UofA with CD22 ligand provided by Dr. Paulson. We will work with the peanut tetramers to study effects of CD22 STALs on the number of peanut-specific B cells.

For Aim 1, Major Task 2: We will continue working with the conferred allergy model to better understand how the Ah1, 2, 3, and 6 STALs are depleting memory B cells. We will utilize the B cell tetramers we optimized in this reporting period. We anticipate publishing these data once we have a clearer picture of mechanistic correlates with the CD STALs in vivo findings.

For Aim 1, Major Task 3: We will continue to utilize our novel NSG mouse model with human B cell engraftment to study the effects of human CD22L peanut allergen STALs on human B cells. We plan to test 5-10 human blood donors in this model.

For Aim 2, Major Task 2: We will assess the CD33 STALs in our human basophil activation assay (BAT). Ah1, 2, 3, and 6 STALs will be prepared by Dr. Paulson's group at TSRI and tested in the BAT assay by Dr. Kulis at UNC. We aim to demonstrate that the combined Ah1, 2, 3, and 6 CD33 STALs can prevent degranulation to whole peanut extract. Once we have obtained more replicates and completed further testing with additional peanut allergens, we plan to write a manuscript and publish our findings.

At TSRI

The project funds have been spent down. We will continue to work with UNC and Dr. Kulis to provide STALs with human CD33L for use in the basophil experiments. We will continue to finish experiments and contribute to publications.

At UofA

The project funds have been spent down. We will continue to work with Dr. Kulis at UNC to provide STALs with either human or mouse CD22L for use in in vivo experiments. We will continue to finish experiments and contribute to publications.

4. IMPACT:

- **What was the impact on the development of the principal discipline(s) of the project?**

Aim 1: Demonstration that STALs targeting CD22 can deplete memory B cells in an adoptive transfer model indicates that utilizing these nanoparticles could be a viable approach to deplete the allergy-causing B cells in allergic individuals. Furthermore, studies with peanut tetramers will allow us to study the effects that STALs have on B cells in vivo (mouse) and ex vivo (humans). The tetramers will be a powerful tool to study peanut-specific B cells in other allergy-related projects, such as clinical trials with oral and sublingual immunotherapy. Development of a novel model to investigate human B cells in vivo using NSG mice repopulated with human PBMCs, we are moving closer to demonstrating effects on human cells and moving towards clinical applications.

Aim 2: Demonstration that STALs can suppress antigen-mediated activation of mast cells and basophils and desensitize mice to subsequent response to antigen challenge suggests the potential for translation to managing treatment of patients exposed to allergens for 'allergen shots' to develop tolerance, or administration of medicines to allergic individuals. Our development of a novel reagent conjugating the hCD33L to anti-human IgE may prove truly important for clinical utility since no liposomes are used and there is no need for allergen-specific strategies, rather this tolerizing agent may work for mast cell and basophils in a non-allergen specific fashion.

- **What was the impact on other disciplines?**

  - Generation of a novel mouse model to study memory B and T cell responses in the absence of circulating antibodies is a valuable model to the field of food allergy research.
  - Generation and optimization of peanut allergen tetramers provides an important set of reagents to track B cell responses to therapies in mouse models and in human patients.
  - Development of a novel mouse model in NSG mice to study human CD22 on human B cells in vivo is an important model to study food allergy and other immunologic diseases.
  - Creation of a novel transgenic mouse with hCD33 expressed on microglial cells will be a valuable tool to study the importance of CD33 as a risk factor in Alzheimer's disease.
  - Creation of a novel reagent coupling human CD33L to anti-human IgE could be a powerful reagent to study tolerance in a non-allergen specific fashion.

- **What was the impact on technology transfer?**

  Licensing the hCD33-Tg mice to pharma companies will facilitate the development of new medicines to treat allergy and Alzheimer's disease

- **What was the impact on society beyond science and technology?**

  Nothing to Report

5. CHANGES/PROBLEMS:

- **Changes in approach and reasons for change**

  There were no significant changes to the approach during the reporting period

- **Actual or anticipated problems or delays and actions or plans to resolve them**

  The major delay in the experiments resulted from COVID-19, which shut down our labs for several months approximately half-way through this reporting period. Mice had to be euthanized and there were substantial delays in getting mice and other reagents once our labs were allowed to operate at half-capacity. We are now back to working on a regular basis with our experiments back up and running at nearly full-capacity. We were granted a second no-cost extension at UNC to continue using the remaining funds on this project. Additionally, we have applied for an Expansion Award using our data generated from this project's funding.

- **Changes that had a significant impact on expenditures**

  COVID-19 delays caused a slowing of expenditures at UNC. We have been granted a second no-cost extension to continue using the remaining funds.

- **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**

  Nothing to Report

- **Significant changes in use or care of human subjects**

  Nothing to Report

- **Significant changes in use or care of vertebrate animals**

  Nothing to Report

- **Significant changes in use of biohazards and/or select agents**

  Nothing to Report

6. PRODUCTS:

- **Publications, conference papers, and presentations**

  Journal publications:

Publications: Eight Peer-Reviewed Publications (Two additional manuscripts in preparation).

1. Exploiting CD22 on antigen-specific B cells to prevent allergy to the major peanut allergen Ara h 2 (2017). Orgel KA, Duan S, Wright BL, Maleki SJ, Wolf JC, Vickery BP, Burks AW, Paulson JC, Kulis MD, Macauley MS. J Allergy Clin Immunol 139(1): 366-369.
2. Human CD22 inhibits murine B cell receptor activation in a human CD22 transgenic mouse model (2017). Bednar KJ, Shanina E, Ballet R, Connors EP, Duan S, Juan J, Arlian BM, Kulis MD, Butcher EC, Fung-Leung WP, Rao TS, Paulson JC, Macauley MS. J Immunol 199(9): 3116-3128.
3. Antigenic liposomes for generation of disease-specific antibodies (2018). Bednar KJ, Hardy L, Smeekens J, Raghuwanshi D, Duan S, Kulis MD, Macauley MS. J Vis Exp 140.
4. A mouse model of peanut allergy induced by sensitization through the gastrointestinal tract (2018). Orgel K, Kulis MD. Methods Mol Biol 1799: 39-47.
5. CD33 recruitment inhibits IgE-mediated anaphylaxis and desensitizes mast cells to allergen (2019). Duan S, Koziol-White CJ, Jester WF, Nycholat CM, Macauley MS, Panettieri RA, Paulson JC. J Clin Invest 129(3): 1387-1401.
6. Exploiting CD22 to selectively tolerize autoantibody producing B-cells in Rheumatoid Arthritis (2019). Bednar KJ, Nycholat CM, Rao TS, Paulson JC, Fung WP, Macauley MS. ACS Chem Biol 14(4): 644-654.
7. Coordinated roles for glycans in regulating the inhibitory function of CD22 on B cells (2019). Enterina JR, Jung J, Macauley MS. Biomed J 42(4): 218-232
8. Duan, S.; Paulson, J. C., Siglecs as Immune Cell Checkpoints in Disease. *Annu Rev Immunol* **2020**.

Books or other non-periodical, one-time publications:

- None

Other publications, conference papers, and presentations

- **Abstracts and presentations at conferences: Michael Kulis (PI)**
  - Invited Oral Presentation – March 2020
    UNC Translational Medicine Program, Chapel Hill, NC
    The University of North Carolina at Chapel Hill
    Title: Using Siglec-engaging Tolerance-inducing Antigenic Liposomes (STALs) to exploit CD22 on peanut-specific memory B cells to induce tolerance.
  - Poster Presentation – March 2020

American Academy of Allergy, Asthma, Allergy, and Immunology.
Online (originally planned to be held in Philadelphia, PA)
Title: Using Siglec-engaging Tolerance-inducing Antigenic Liposomes (STALs) to exploit CD22 on peanut-specific memory B cells to induce tolerance.

- **Website(s) or other Internet site(s)**

  Nothing to Report

- **Technologies or techniques**

  At TSRI an additional novel strain of transgenic mice was created using the Rosa26-hCD33 strain we had used to develop the strain with hCD33 expressed in mast cells described in Aim 2, Task 3. The new strain of mice has hCD33 expressed in brain microglial cells, and is of particular utility for the study of the roles of microglial cells in Alzheimer's disease

Inventions, patent applications, and/or licenses

TSRI has licensed the novel strain of transgenic mice with hCD33 expressed in microglial cells to one pharmaceutical company, and is in the process of licensing these mice to a second pharmaceutical company

- **Other Products**

  Nothing to Report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS:

- **What individuals have worked on the project?**

University of North Carolina – Chapel Hill (UNC)

Mike Kulis, PhD (Initiating PI) – unchanged

Rishu Guo, PhD (Research Scientist) – unchanged

Johanna Smeekens, PhD (Postdoc Scientist) – Unchanged

Lakeya Hardy (Grad Student) – unchanged

Kelly Orgel (Grad Student) – unchanged

Jada Suber (Grad Student) – unchanged

Xiaohong Yue (Research Associate) – unchanged

The Scripps Research Institute (TSRI)

James C. Paulson (Partnering PI) – unchanged

Shiteng Duan (Grad Student) – unchanged (last day worked July 26, 2019)

Kevin Worrell (Research Assistant) – unchanged

Joana Juan (Research Assistant) – unchanged (last day worked April 26, 2019)

Name:	Jasmine Stamps
Project Role:	Research Assistant
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	2
Contribution to Project:	Replacement for Joana - performed all the mouse genotyping and helped setup the appropriate mouse breeders. Also performed retro-orbital bleeds and analyzed antibody titers by ELISA

Funding Support:	N/A

University of Alberta (UofA)

Matthew Macauley (Subcontractor) – unchanged

Susmita Sarkar (Research Technician) – unchanged

Maju Joe (Post Doctoral Associate) – last day worked September 1, 2018

Dharmendra Raghuwanshi (Post Doctoral Associate) – last day worked October 1, 2018

Name:	Kelli McCord
Project Role:	Graduate Student
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	6
Contribution to Project:	Preparing antigen and liposomes
Funding Support:	N/A

Name:	Gour Daskan
Project Role:	Postdoctoral fellow
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	6
Contribution to Project:	Linking glycans (provided by Paulson lab) to lipid
Funding Support:	N/A

- **Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

  For Dr. Kulis at UNC, nothing significant to report

  For Dr. Paulson is the Partnering Investigator at TSRI
  - NIH grant #R01AI050143 ended 09/30/2019; #P01HL107151 ended 05/30/2019; UM1AI100663 ended 06/30/2019
  - NIH Grant R01AI132790 was funded 09/24/2018; UM1AI144462 was funded 07/01/2019

  For Dr. Macauley at UofA a sub-contract to Dr. James Paulson, no significant change in overall effort devoted to the project.

- **What other organizations were involved as partners?**

  Organization Name: University of Alberta (UofA)
  11227 Saskatchewan Drive, Edmonton, Alberta, Canada T6G 2G2 (foreign)
  Subcontractor PI: Matthew Macauley, PhD

8. SPECIAL REPORTING REQUIREMENTS:

- **COLLABORATIVE AWARDS:**
  Dr. Paulson (Partnering PI) will submit a Final Report this reporting period as he has spent down all of the funding for this award.

- **QUAD CHARTS:**
  Not applicable

9. APPENDICES:
Not applicable